

What is claimed is:

1. A method for controlling the transcription of target genes, the method comprising:
  - 5 identifying at least one logic function having an output corresponding to a desired target gene output signal; and
  - implementing the at least one logic function by producing interactions among a plurality of regulatory proteins and interactive binding of two or more regulatory proteins at corresponding binding sites of the target genes, wherein the target genes
  - 10 each comprise one or more cis-regulatory sequences having individual DNA binding sites, and wherein each binding site has a binding strength and a binding location which are adjustable by varying composition of the one or more cis-regulatory sequences;
  - wherein the interactions comprise contact and long-distance interactions.
  - 15
2. The method of claim 1, wherein the cis-regulatory region is modular.
3. The method of claim 1, wherein the at least one logic function is selected from the group consisting of: OR, AND, NAND, XOR and EQ.
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4. The method of claim 1, wherein at least some of the interactions among the regulatory proteins comprise non-specific protein-protein interactions controlled by selecting the binding locations.
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5. The method of claim 1, wherein at least some of the interactions among the regulatory proteins comprise specific protein-protein interactions.
6. The method of claim 1, wherein at least some of the interactions among the regulatory proteins comprise effective protein-protein interactions mediated by
- 30 collaborative competition between the regulatory proteins and a generic DNA-bound protein or protein complex.

7. The method of claim 1, wherein the interactive binding comprises tunable-specific protein-DNA interactions which are tunable by selecting the binding strengths.

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8. The method of claim 1, wherein the cis-regulatory region includes long distance repression and activation schemes.

9. The method of claim 1, further comprising, after the step of identifying the  
10 at least one logic function:

reducing the at least one logic function to a minimal conjunctive normal form;  
and

implementing a first clause as an activation clause and all remaining clauses as repression clauses;

15 wherein the relative binding strength is selected so that repression dominates activation.

10. The method of claim 1, further comprising, after the step of identifying the at least one logic function:

20 reducing the at least one logic function to a minimal disjunctive normal form;  
and

implementing a first clause as a repression clause and all remaining clauses as activation clauses.

25 11. A method for genetic computing using combinatorial transcription control for controlling gene expression, the method comprising:

identifying at least one logic function having an output corresponding to a desired gene expression; and

30 implementing the at least one logic function by producing interactions among a plurality of transcription factors and interactive binding of two or more transcription factors at corresponding binding sites of one or more target genes, wherein the target

genes each comprise one or more cis-regulatory regions having individual DNA binding sites, and wherein each binding site has a binding strength and a binding location which are adjustable by varying composition of the one or more cis-regulatory sequences.

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12. The method of claim 11, wherein the cis-regulatory region is modular.

13. The method of claim 11, wherein the at least one logic function is selected from the group consisting of: OR, AND, NAND, XOR and EQ.

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14. The method of claim 11, wherein at least some of the interactions among the transcription factors comprise non-specific protein-protein interactions controlled by selecting the binding locations.

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15. The method of claim 11, wherein at least some of the interactions among the transcription factors comprise specific protein-protein interactions.

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16. The method of claim 11, wherein at least some of the interactions among the transcription factors comprise effective protein-protein interactions mediated by collaborative competition between the transcription factors and a generic DNA-bound protein or protein complex.

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17. The method of claim 11, wherein the interactive binding comprises tunable-specific protein-DNA interactions which are tunable by selecting the binding strengths.

18. The method of claim 11, wherein the cis-regulatory region includes a long distance repression and activation schemes.

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19. The method of claim 11, further comprising, after the step of identifying the at least one logic function:

reducing the at least one logic function to a minimal conjunctive normal form;  
and

implementing a first clause as an activation clause and all remaining clauses as  
repression clauses;

5        wherein the binding strength is selected so that repression dominates  
activation.

20. The method of claim 11, further comprising, after the step of identifying  
the at least one logic function:

10        reducing the at least one logic function to a minimal disjunctive normal form;  
and

implementing a first clause as a repression clause and all remaining clauses as  
activation clauses.

15        21. A method of encoding control functions in regulatory DNA sequences  
comprising:

selecting a relative binding strength and a relative binding position of  
individual binding sites within a cis-regulatory region of the regulatory DNA  
sequence to operate as at least one logic function for generating an output upon  
20        binding corresponding to a desired gene expression.

22. The method of claim 21, wherein the control functions are modular.

23. The method of claim 21, wherein the relative binding strengths and  
25        relative binding sites within the cis-regulatory region are selected to produce tunable  
specific DNA-protein interaction and non-specific, glue-like protein-protein  
interaction.

24. The method of claim 23, further comprising selecting the relative binding  
30        strengths and relative binding sites to permit distal activation and repression.